Effects of Subanesthetic Ketamine on Pain and Cognitive Functions in TIVA

TİVA'da Subanestezik Ketaminin Ağrı ve Kognitif Fonksiyonlara Etkisi

TIVA'da Subanestezik Ketamin / TIVA with Subanesthetic Ketamine

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Özet

Amaç: TIVA ile laparoskopik kolesistektomi yapılması planlanan hastalarda, subanestezik dozda uygulanan ketaminin analjezik tüketimi, kognitif fonksiyonlar, perioperatif hemodinami ve postoperatif derlenme üzerine etkilerinin karşılaştırılması amaçlandı. Gereç ve Yöntem: Hastane Etik Kurul onayı ve hastaların yazılı izinleri alındıktan sonra, elektif laparaskopik kolesistektomi yapılması planlanan 20-70 yaş arası ASAI-III 60 hasta rastgele 30'arlı iki gruba ayrıldı. Operasyon öncesinde her iki gruba da Mini Mental Test (MMT) uygulandı. Grup 1'e (TİVA-Ketamin) indüksiyondan 2dk önce 0,25mg.kg-1 ketamin IV uygulandı. Takiben her iki gruba da indüksiyonda (Grup 1 (TİVA-Ketamin) ve Grup 2'ye (TİVA)) 2mg.kg-1 propofol, 1µg.kg-1 fentanil IV ve 0,6 mg.kg-1 rokuronyum IV; idamede 5-8mg.kg-1.sa-1 propofol, 0,15µg.kg.-1 remifentanil IV, %50 O_2-hava verildi. Postoperatif ağrı takibi IV tramadol (PCA) ile sağlandı. 24 saatlik toplam doz kaydedildi. Operasyon boyunca hemodinamik parametreler, ekstübasyon, göz açma, komutlara yanıt verme ve oryantasyon zamanları kaydedildi. Ekstübasyon sonrası Ramsey Sedasyon Skorları (RSS) ve Aldrete Derlenme Skorları (ADS) kaydedildi. Postoperatif 24. saatte tekrar MMT uygulandı. Bulgular: Gruplar arasında hemodinamik parametreler benzer bulundu. Ketamin yapılan hastalarda toplam analjezik tüketimi anlamlı düzeyde düşük bulundu (p<0,01). ADS 5 ve 10. dk'larda ketamin yapılan grupta daha düşük bulundu (p=0,05). RSS'de ketamin yapılan grupta daha yüksekti (p=0,05). Ekstübasyon, komutlara uyma ve oryantasyon zamanları ketamin yapılan grupta daha uzun bulundu (p=0,05). MMT; başlangıç ve 24. Saat değerleri arasında ve hasta memnuniyetleri açısından gruplar arasında fark yoktu (p>0,05). Tartışma: Total intravenöz anestezide ketamin ilavesinin intraoperatif hemodinami üzerine olumsuz etkisi olmamış, daha etkin postoperatif analjezi sağlanmıştır ancak uyanma ve derlenme süresini uzattığı için erken dönemde daha dikkatli takip gerektiğini düşünmekteyiz.

Anahtar Kelimeler

Ketamin; Kognitif Bozukluklar; İntravenöz Anestezi

Abstract

Aim: It was aimed to compare the effects of subanesthetic dose ketamine on analgesic consumption, cognitive functions, perioperative hemodynamics and postoperative recovery in patients scheduled for laparoscopic cholecystectomy under total intravenous anesthesia (TIVA). Material and Method: The study was approved by Institutional Ethics Committee and all patients gave written informed consent. Sixty ASA I-III patients aged 20-70 years scheduled for elective laparoscopic cholecystectomy were randomly assigned into 2 groups [group 1 (TIVA-ketamine) and group 2 (TIVA)]. Both groups underwent Mini Mental Test (MMT) before the operation. In the group 1, 0.25 mg.kg-1 ketamine was given 2 minutes before induction via intravenous route. Anesthesia was induced by using 2mg.kg-1 propofol, 1µg.kg-1fentanyl (iv) and 0.6 mg.kg-1 rocuronium (iv) in both groups. Anesthesia was maintained by 5-8mg.kg-1.h-1 propofol, 0,15µg kg-1 remifentanil (iv) and 50:50 mixtures of O2 and air. Postoperative pain management was achieved by tramadol HCl via patient-controlled analgesia (PCA) device. Total dose within 24 hours was recorded. Hemodynamic parameters during surgery and times to extubation, eye opening, receiving verbal commands and orientation time were recorded. Ramsey sedation score (RSS) and Aldrete recovery score (ARS) were recorded after extubation. MMT was repeated on the postoperative hour 24. Results: Hemodynamic parameters were found to be similar in both groups. Total analgesic consumption was found to be significantly lower in patients received ketamine (p<0.001). ARSs on minutes 5 and 10 were found to be lower in ketamine group (p=0.05). RSSs were found to be higher in ketamine group (p=0.05). Times to extubation, receiving verbal commands and orientation were found to be longer in ketamine group (p=0.05). There was no significant difference regarding baseline and postoperative values of MMT as well as patient satisfaction between groups (p>0.05). Discussion: Addition of subanesthetic dose ketamine to total intravenous anesthesia had no adverse effect on intraoperative hemodynamic parameters; it provided more effective postoperative analgesia; however, we think that a meticulous monitoring is required during early postoperative period as it prolonged awakening and recovery times.

Keywords

Ketamine; Anesthesia Intravenous; Cognition Disorders

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Introduction

Anaesthesia practice is developing with new generation drugs but we have some basic drugs such as thiopental sodium, morfin and ketamine which never olds. On the other hand, in recent 10 years, ketamine was not popular as it was in the past. That's why, with having strong negative prejudice because of the possible side effects, new generation anesthesiologists were not familiar with ketamine during the anaesthesia practise. But we all know that, besides its side effects, ketamine is still unique and indispensable drug.

Provision of early recovery and rapid normalization of cognitive functions are major criterias in the selection of agents in anesthesia practice. It is known that ketamine use at anesthetic doses affects cognitive functions, but with the new drug combinations such as remifentanyl, dexmedetomidine and propofol, studies evaluating the effects of subanesthetic doses ketamine on cognitive functions are limited. And also, some beneficial effects have been detected on recovery, hemodynamics and postoperative analgesic consumption by subanesthetic doses used before induction [1-3].

Anesthetic agents affect functions of central nervous system in many degrees. After cessation of anesthesia, it takes time for returning of psychomotor functions to preoperative levels. Psychomotor dysfunction after anesthesia is termed as postoperative cognitive dysfunction (POCD) [4]. It can be assessed by Mini Mental Test (MMT), which depends on subjective data and can be performed in a short time period at bedside [5].

Total intravenous anesthesia (TIVA) is increasingly used in anesthesia practice as it provides better hemodynamics and recovery when compared to inhalation anesthesia. In TIVA, propofol and remifentanil infusions are preferred due to their shorter time of action [6].

In the present study, we aimed to investigate the effects of subanesthetic dose ketamine on hemodynamic parameters, recovery, postoperative analgesia and cognitive functions in patients scheduled to laparoscopic cholecystectomy under total intravenous anesthesia with propofol-remifentanil infusions.

Material and Method

This study was approved by Local Ethics Committee on 28 April 2011 under supervision of chairperson Prof Goçmen with the number of "6206" and all patients gave written informed consent before the recruitment. This is a single-center, double-blinded, balanced randomized (1:1), prospective study conducted at Anesthesia Department of Umraniye Training and Research Hospital.

Overall, 60 patients with American Society of Anesthesiologists (ASA) I-III who scheduled to elective laparoscopic cholecystectomy were included to the study. The patients were randomly assigned into two groups as follows: group 1 (TIVA-ketamine) and group 2 (TIVA). All patients were informed about surgery on the day before surgery and underwent MMT (2). The patients with severe neurological disease, those with renal, hepatic, pulmonary insufficiency or cardiac failure, those with chronic alcoholism and substance abuse, analphabet patients, those considered to be unable to use patient-controlled analgesia (PCA) device and those received anesthesia within prior 7 days were excluded.

Randomization was performed by a simple randomization procedures using computerized-random numbers generator. Patients were randomly assigned to one of 2 groups according to ketamine administration with 1:1 allocation using a group size of 30. Random number list preparation, random number list assignment to groups, drug administration and evaluation of analgesic consumption and MMT were performed by different anesthesiologists. Both care providers on the ward and the anesthesiologists assessing outcomes were blinded to the study groups.

Without premedication, standard monitoring was performed at operation room. Before induction, heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), means arterial pressure (MAP, peripheral oxygen saturation (SpO2) values were recorded at baseline.

Two minutes before induction, patients in group 1 received 0.25 mg kg-1 ketamine in normal saline (2 cc in total) (iv), whereas patients in group 2 received same amount of normal saline (iv). A nurse who didn't involve in the study prepared the drugs. The anesthesia induction was achieved by using 2mg kg-1 propofol, 1µg kg-1 fentanyl (iv) and 0.6 mg kg-1 rocuronium (iv) in both groups. The anesthesia was maintained by 6mg kg-1h-1 propofol, 0.15 µg kg-1.min-1 remifentanil (iv) and 50:50 mixture of O2 and air. Patients were closely monitored regarding hemodynamic parameters. The remifentanil was titrated by 0.05µg. kg-1.min-1 dose intervals in case of HR alteration by 15 % and SAP by 20 %. The HR, SAP, DAP, MAP, SpO2 and end-tidal carbon dioxide (ETCO2) values were recorded before intubation and on the minutes 1, 3, 5, 10, 15 after intubation and at every 15 minutes thereafter until the end of operation in all patients.

All patients received 1 mg kg-1 tramadol HCl 30 minutes before completion of surgery for analgesia. After completion of skin closure, all anesthetic agents were withdrawn. Then, 0.01 mg kg-1 atropine and 0.04 mg kg-1 neostigmine were given to reverse neuromuscular blockage. Times to extubation, eye opening, receiving verbal command and orientation time were recorded. RSS and ARS were assessed on the minutes 5, 10 and 15 after extubation. Patients stayed in recovery room for 1 hours and hemodynamic parameters were recorded including HR, SpO2 SAP, DAP and MAP. Intravenous PCA device was used in the recovery room with following parameters: concentration, 5 mg ml-1; bolus dose, 10 mg; lock-out, 12 minutes. The patients were instructed to use button when he/she experienced pain. Total tramadol HCl consumption within 24 hours was recorded. Demographic and hemodynamic data, recovery time, total analgesic consumption within 24 hours, preoperative and postoperative MMT scores and preoperative and postoperative complications were recorded.

Statistical Analysis

In the power analysis, according to a pilot study in 10 patients in each group for the MMT assessment, the minimum sample size was calculated as 27 patients in each group for power of 80 % and alpha value of 0.05 when delta value and SD was taken as 1 and 1.3 units, respectively.

In the power analysis, according to a pilot study for 10 patients in each group for the average of 24-hours total tramadol dose, the minimum sample size was calculated as 27 patients in each group for power of 95 % and alpha value of 0.01 when delta va-

lue and SD was taken as 150 and 130 units, respectively.
Number Cruncher Statistical System (NCSS) 2007&PASS 2008 Statistical Software (Utah, USA) program was used for the statistical analysis. During analyses of data obtained from the study, descriptive statistical methods of mean, standard deviation, frequency and ratio values were used in the tables. Student's t test was used for intergroup comparisons, whereas chi-square test was used to compare quantitative variables. p<0.05 was considered as significant.

Results

Of the patients, 39 didn't meet inclusion criteria, while 3 patients declined to participate to the study. Overall, 60 patients participated and completed the study.
There was no significant difference between groups regarding age, gender, weight, duration of operation and ASA scores (p>0.05; Table 1).

Table 1. Demographic characteristics of the groups

		Group 1 Mean ±SD	Group 2 Mean ± SD	+p
Age (years)		46.03±12.29	46.96±11.54	0.765
Height (m)		1.63±0.07	1.61±0.06	0.289
Weight (kg)		78.53±10.60	76.67±13.23	0.549
Duration of surgery (min)		69.50±11.75	63.53±12.93	0.067
		n (%)	n (%)	++p
Gender	Female	22 (73.3%)	27 (90%)	0.095
	Male	8 (26.7%)	3 (10%)	
ASA*	I	18 (605)	17 (58.6%)	0.914
	II	12 (40%)	12 (41.4%)	

+ Student t test
++Chi-square test
*ASA: American Society of Anaesthesiology

No significant difference was found in MAP measurements at preoperative, perioperative and postoperative periods between groups (p>0.05; Figure 1, 2).

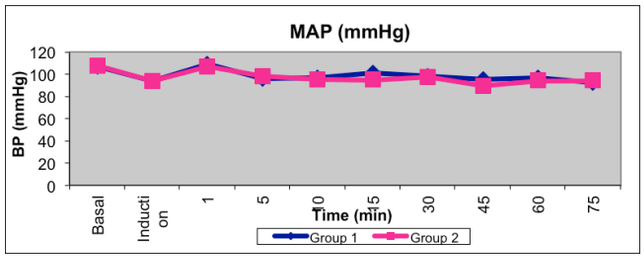

Figure 1. Perioperative MAP* values in groups
*MAP: Mean Arterial Pressure

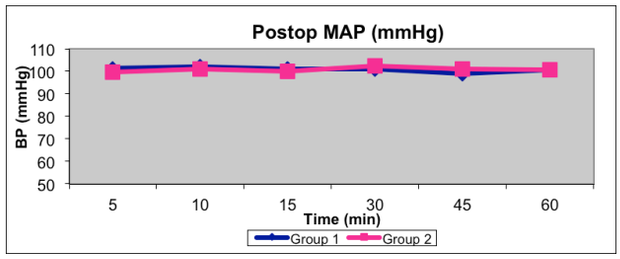

Figure 2. Postoperative MAP values in groups
*MAP: Mean Arterial Pressure

Measurements of HR also found to be similar at preoperative, perioperative and postoperative periods between groups (p>0.05; Figure 3,4).

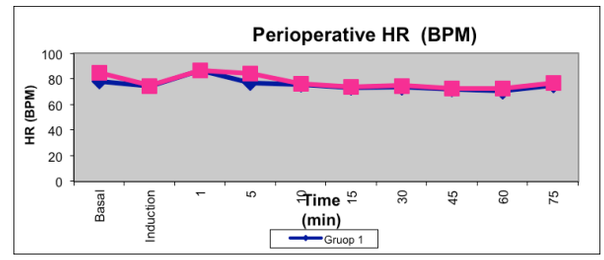

Figure 3. Perioperative HR* values in groups
*HR: Heart Rate

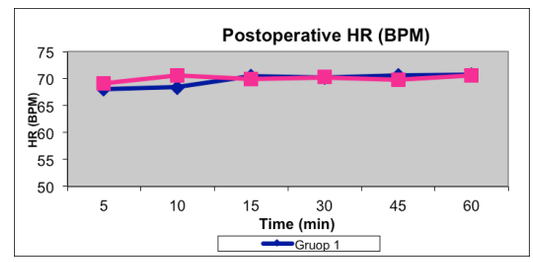

Figure 4. Postoperative HR* values in groups
*HR: Heart Rate

Times to extubation, eye opening, receiving verbal commands and orientation were found to be significantly longer in-group 1 when compared to group 2 (p<0.01; Table 2).

Table 2. Times to extubation, eye opening, receiving verbal commands and orientation in groups (Mean ± SD)

	Group 1 Mean ±SD	Group 2 Mean ±SD	+p
Extubation (min)	9.03±2.12	5.53±1.47	0.001**
Eye opening (min)	9.63±2.25	5.96±1.47	0.001**
Receiving verbal command (min)	10.96±2.41	7.50±1.79	0.001**
Orientation (min)	15.40±3.11	11.16±2.07	0.001**

+ Student's t test
**p<0.01

No significant difference was found in MMT values obtained at preoperative period between groups. Again, MMT values obtained on the hour 24 after surgery were also similar between groups (p>0.05; Table 3).

Table 3. Assessment of groups according to MMT* values

MMT	Group 1 Mean ±SD	Group 2 Mean ±SD	+p
Preoperative	27.78±1.19	27.43±1.50	0.330
On the hour 24	27.93±1.94	28.66±1.32	0.093

+ Student's t test
*MMT: Mini Mental Test

In the recovery room, Aldrete score measurements on the minute 5 were significantly higher in group 2 when compared to group 1 (p<0.01). Again, Aldrete score measurements on the minute 10 were found to be significantly higher in group 2 (p<0.05) (Figure 5).

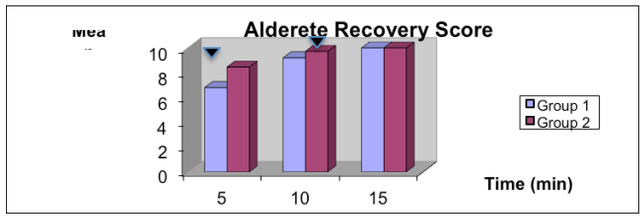

Figure 5. Assessment of ADS* between groups
p <0.01 inter-group comparisons (student t test)*ARS: Aldrete Recovery Score

In the group 1, Aldrete score ≥9 values were detected in 4 patients (13.3%) on the minute 5, in 21 patients (70%) on the minute 10 and in 5 patients (30%) on the minute 15, whereas in 19 patients (63%) on the minute 5, in 9 patients (30%) on the minute 10 and in 2 patients on the minute 15 in group 2.

When RSS values were compared between groups, it was found that RSS values on the minute 5 were significantly higher in group 1 than group 2 (p<0.01), while RSS values on the minute 10 and 15 were similar between groups (Figure 6).

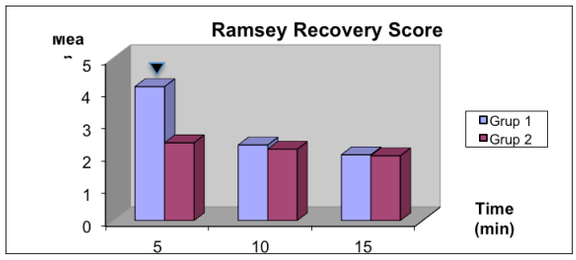

Figure 6. Assessment of RSS* between groups
p<0.01 inter-group comparisons (Mann-Whitney U test) * RSS: Ramsey Sedation Score

While perioperative tramadol and remifentanil doses were similar between groups, tramadol dose given by PCA device was significantly lower in group 1 (p<0.01; Table 4).

Table 4. Analgesic consumption

	Group 1 Mean ±SD	Group 2 Mean ±SD	+p
Amount of perioperative tramadol (mg)	81.83±11.48	79.50±13.91	0.482
Amount of perioperative remifentanil (mcg)	0.97±0.24	0.85±0.28	0.081
Amount of tramadol during 24-hours PCA* (mg)	216.66±105.44	370.83±95.28	0.001**

+ Student's t test
**p<0.01 inter-group comparisons
*PCA: Patient Controlled Analgesia

The complications and complication rates in groups are shown in Table 5. There was no significant difference between groups regarding complications and no significant difference between groups regarding patient satisfaction (p>0.05; Table 6).

Discussion

Total intravenous anesthesia is widely used as it has rapid onset of action and provides rapid awakening and better hemodynamic control when compared to inhalation anesthesia. In TIVA, short-acting opiates can be used as additional agents to provide analgesia and to reduce the amount of anesthetic agent infused [7]. Ketamine is an agent in phencyclidine group, which inhibits postsynaptic NMDA receptor via glutamate and disrupts connection between thalamus, which transmits sensorial stimuli from reticular formation to cerebral cortex, and limbic cortex that accounts from these sensorial stimuli [8]. In this anesthesia type, termed as dissociative anesthesia, patient can open his/her eyes, but cannot perceive sensorial stimuli. Ketamine use is limited due to its known adverse effects such as perioperative hallucination and postoperative cognitive dysfunction.

Table 5. Distribution of complications

	Group 1 n (%)	Group 2 n (%)	+p
Vomiting	8 (26.7%)	5 (16.7%)	0.347
Bradycardia	2 (10%)	2 (6.7%)	1.000
Hypotension	2 (6.7%)	1 (3.3%)	1.000
Sweating	4 (13.35)	2 (6.7%)	0.671
Tachycardia	2 (6.7%)	0 (0%)	0.492
Nausea	11 (36.7%)	7 (23.3%)	0.399

+Chi-square test

Table 6. Assessment of groups according to patient satisfaction

Patient satisfaction	Group 1 n (%)	Group 2 n (%)	P
Very good	7 (23.3%)	7 (23.3%)	0.665
Good	14 (46.7%)	17 (56.7%)	
Moderate	8 (26.75)	6 (20%)	
Poor	1 (3.3%)	0 (0%)	

+Chi-square test

In our study, the effects of adding subanesthetic dose ketamine during anesthesia induction in TIVA on perioperative hemodynamic parameters, postoperative recovery, postoperative analgesic consumption and cognitive functions were investigated in patients undergoing elective laparoscopic cholecystectomy.

The ketamine is the only intravenous anesthetic agent that has stimulant effect of cardiovascular system on contrary to other known anesthetic agents. It increases arterial blood pressure and heart rate by 30% [9,10].

In a study by Güneş et al [3] in which they used perioperative propofol (4-6 mg kg-1 h-1) with alfentanil (1 mg kg-1min-1) vs. propofol (2 mg kg-1 h-1) with alfentanil (0.5mg.kg-1 min-1) with ketamine (0.5 mg kg-1 h-1) in 30 patients aged 27-65 years undergoing laminectomy, no significant differences was found in perioperative hemodynamic parameters between groups [3]. Although ketamine was only given 2 minutes before induction in our study on contrary to the study by Güneş et al., no significant differences was detected in inter-group and intra-group comparisons regarding hemodynamic parameters which was found to be in normal range. We attributed these findings to use of ketamine at subanesthetic doses in both studies.

Tissue injury occurring surgery alters central process pathway of pain perception. These alterations reduce stimulation threshold and enhance postoperative pain. The initiation and maintenance of the central sensitization could be based on NMDA receptors. Thus, it has been reported that use of ketamine (a NMDA receptor antagonist) before surgery may prevent central sensitization and reduce intraoperative analgesic require-

ment as well as it may contribute to relieve of postoperative pain [3,6-11].

In a study on 50 patients received desflurane-remifentanil anesthesia by Guignard et al. [12] patients received 0.15 mg kg-1 ketamine bolus followed by 2 μg kg min-1 ketamine infusion. Authors found that remifentanil requirement was smaller in ketamine group when compared to controls. In addition, it was found that time to first analgesic (morphine) need was longer and total morphine consumption within 24 hours was lower in the ketamine group [12] .

In a study on 50 children underwent adenotonsillectomy by Aspinal et al. [13], it was reported that preoperative ketamine (0.05 mg kg-1) administration provided an equivalent analgesia to morphine without leading postoperative adverse effects; in addition, ketamine was a safer agent in patients at risk for postoperative airway obstruction.

In a study on 155 patients underwent laparoscopic gynecologic procedures by Kwok et al. [2], ketamine (0.15 mg kg-1) was given before surgical incision to patients and it was found that pain scores within first 6 hours were lower while time to first analgesic need was longer in ketamine group than controls.

In our study, there was no significant difference between ketamine and control group regarding the amount of remifentanil and tramadol HCl used during surgery; however, tramadol HCl consumption within first 24 hours after surgery was lower in ketamine group than controls in agreement with previous studies ($p<0.01$).

There are several studies that evaluated the effect of timing of ketamine administration on postoperative analgesic effectiveness.

C. Menigaux et al. [14] investigated analgesic effectiveness of intraoperative ketamine use in patients scheduled to arthroscopic repair of anterior cruciate ligament. Authors assigned the patients into 3 groups as follows: the PRE group received 0.15 mg kg-1 ketamine before surgical incision whereas POST group received the same dose of ketamine at the end of surgery. CONT group received normal saline either before or after surgery. Postoperative morphine consumption was found to be markedly lower in both groups received ketamine when compared to controls. Authors concluded that single dose intraoperative ketamine administration at both time points prolonged the time to first analgesic need and reduced total morphine consumption by 50% within first 48 hours [15].

In a study on 45 patients aged 5-15 years undergoing tonsillectomy, Özgün et al. [15] administered subanesthetic ketamine doses at different time points. Ketamine infusion (6 mg kg-1 min-1) was administered from preemptive period until bleeding control in one group, while ketamine (0.8 mg kg-1) was given during bleeding control in the other group. VAS scores and total paracetamol consumption within first 6 hours were found to be lower in the group received ketamine at preemptive period.

In our study, we preferred to administer ketamine 2 minutes before the induction due to positive effects on postoperative analgesic consumption, as in the study by Özgün et al.

It is known that ketamine has delaying effect on awakening and recovery. Ostreikov et al. [16] compared awakening from general anesthesia after induction by using midazolam, propofol and ketamine in 75 children aged 6-12 years undergoing adenoidectomy. Authors found that awakening was delayed in cases received ketamine and time to awakening from general anesthesia prolonged by dose escalation.

In our study, times to extubation, eye opening, receiving verbal commands and orientation were significantly longer in group 1 than group 2 in agreement with literature ($p<0.01$).

For the patients, Aldrete recovery score should be 9 or higher to prevent postoperative complications and to be discharged from recovery room. In a study on 66 patients aged 20-65 years, Aydın et al. [17] compared the effects of 2.5 mg kg-1 propofol and 2.5 mg kg-1 propofol with 0.5 mg kg-1 ketamine on hemodynamics, analgesia and postoperative recovery. Authors found that Aldrete recovery scores on the minutes 10 and 15 were lower in the ketamine group. Although ketamine was used in lower doses in our study than those used in the study by Aydın et al., Aldrete recovery scores on the minutes 5 ($p<0.01$) and 10 ($p<0.01$) were found to be lower. This was attributed to sedative, amnestic and analgesic effects of ketamine, which is potent even in small doses; thus, leading to depressed activity and awareness. Therefore, one should wait for complete recovery of respiration, activity, awareness and orientation of the patients who received ketamine, even in small doses, when discharging the patient from recovery room according to Aldrete scores. Our findings were in agreement with those by Aydın et al.

Impairment in cognitive functions after surgery is termed as postoperative cognitive dysfunction. Factors having role in the assessment of cognitive functions include surgery type, duration of surgery, anesthesia depth and timing of test. It has been shown that psychomotor and cognitive function can be impaired over 10-12 hours after exposure to anesthetic substances and this impairment may last up to 1-2 days in sensitive tests [18,19].

It has been reported that different ways of ketamine use with different doses have negative effects on verbal memory in several studies [20-22].

Mini Mental Test is a frequently used test to measure cognitive function, which can be applied either in outpatient basis or bedside. It has 5 main fields including orientation, registration memory, attention and recall, calculation and language and total score is 30 [5].

There are many studies evaluating effects of general anesthetics on cognitive functions in the current literature. In the studies evaluating cognitive functions by using different agents such as desflurane-sevoflurane [23], desflurane-TIVA [22], it was reported that MMT values decreased on the hour 1 when compared to baseline values and returned to baseline values on the hour 24. [23,25]. Also It was reported that MMT values returned to baseline on the hour 3 in 85 % of the patients [23].

In our study, there was no significant difference between preoperative and postoperative (on the hour 24) MMT scores. MMT scores on the hour 24 were higher in ketamine group when compared to controls; however, the values were within normal range.

In our study, incidences of nausea, vomiting, bradycardia, hypotension, sweating and tachycardia were similar. In addition, patient satisfaction was also similar among groups. In TIVA group, 70 % of the patients rated the procedure as good or very good, while this rate was 80% in TIVA-ketamine group.

Limitations

In our study, we could not perform the long term outcomes on cognitive functions and neurophatic pain due to discharge protocol of general surgery clinic in our hospital.

Conclusion

In our study, it was concluded that subanesthetic doses of ketamine during TIVA provides hemodynamic stability; reduces postoperative analgesic need; and may delay the recovery by enhancing sedation at early period.

Competing interests

The authors declare that they have no competing interests.

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